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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/865,759	05/25/2001	Phyllis Shapiro	708-4057	4368

27123 7590 04/17/2006
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EXAMINER

SMITH, CAROLYN L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 04/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/865,759

Applicant(s)

SHAPIRO, PHYLLIS

Examiner

Carolyn L. Smith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission, filed 1/17/06, has been entered.

Amended claims 1-3, 9-10, and 12, filed 1/17/06, are acknowledged.

Claims herein under examination are 1-3 and 5-24.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-14, and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

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NEW MATTER

The amended limitation “without separation of said red blood cells from said extracellular heme-colored blood substitute prior to analysis” in claims 1 and 9 does not have written support in the specification, claims, and/or drawings, as originally filed.

Therefore, the introduction of this phrase is considered to be NEW MATTER. Claims 2-3, 5-8, 10-14, and 24 are also rejected due to their direct or indirect dependency from instant claims 1 and 9.

Applicant argues that a skilled artisan would unambiguously understand the applicant was in possession of embodiments wherein a sample is analyzed on a cell-by-cell hematology analyzer without prior separation of cellular and extracellular components and argues that there is no separating step anywhere in the specification. This statement is found unpersuasive as the originally filed application is silent regarding analyzing without separation and therefore provides no written support for this limitation. It is noted that a positive or negative limitation can offer adequate written support for such a limitation; however, in the instant case, the originally filed application does not mention such separation or lack thereof. Applicant argues that her reference to well known hematology analyzers which are recognized as not requiring prior separation of sample components, such as in paragraph [0026] of the specification, is an implicit disclosure of this without separation feature. This statement is found unpersuasive as this paragraph recites performing analysis on total hemoglobin content which fails to provide adequate written support for analyzing without separation. Applicant argues that Example 1 explicitly states extracellular hemoglobin was added to blood samples before analysis which is the antithesis of prior separation of components. This statement is found unpersuasive there is

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no mention of analysis without separation. Furthermore, adding something to a sample does not provide written support for “without separation” as the two concepts hold different meanings.

Applicant’s arguments are deemed unpersuasive for the reasons given above.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-14, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 9 recite “*analyzing* said blood sample on an automated cell-by-cell hematology analyzer without separation of said red blood cells from said extracellular heme-colored blood substitute prior to *analysis*” which lacks clarity. It is unclear if the last word in this phrase “analysis” is referring to the analyzing at the beginning of the phrase or some other analysis in the method. This unclarity results in a disconnect between the analyses being performed as the “prior to analysis” is not necessarily analysis performed on or by the analyzer. Clarification of this issue via clearer claim wording is requested. Claims 2-3, 5-8, 10-14, and 24 are also rejected due to their dependency from claims 1 and 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3 and 5-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chupp et al. (P/N 5,631,165) in view of Chang et al. (P/N 5,200,323), Samsouondar (WO 98/39634), and Rodriguez et al. (P/N 6,228,652).

Chupp et al. teach a system where information about the blood sample, generally whole blood which comprises red blood cells (with intracellular hemoglobin), is entered into the controller of an automated system that activates the analyzers, including a hematology analyzer, to perform analyses under the direction of the controller (col. 10, lines 54-67 and col. 12, lines 1-9). Chupp et al. describe tests can be performed on the instrument without separating cells from the sample during any phase of the analyses (col. 7, lines 40-46) which represents analyzing via a cell hematology analyzer without separating cells from the sample prior to analysis, as stated in instant claims 1 and 9. Chupp et al. describe the system as including an analyzer module, a data station module, and a pneumatic unit (col. 11, lines 27-29). The data station module has “sufficient software algorithms to manipulate measured data, calculate parameters and display results in a variety of formats” (col. 11, lines 62-67). Chupp et al. further discuss the analyzer module in which sample tubes of blood are automatically transported with bar code labels that

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can be read with a bar code reader so that sample information can be inputted into the system controller (col. 25, lines 22-35) as stated in instant claims 1, 9, 12-13, 15, and 19-20. Chupp et al. teach correcting MCH and MCHC in blood (as stated in instant claims 1, 9, and 21-23) by performing the mathematical computations described in (b) through (e) of instant claim 1 and c(1) – (2) of instant claim 9 where the constants to correct dimension units for formula 1 is 10 and for formula 2 is 100 (col. 53, lines 66-67 and col. 54, lines 1-26), as stated in instant claims 14 and 24. Chupp et al. teach the use of setting hemoglobin flags if any results are abnormal or suspect (col. 61, lines 50-51) which suggests the blood sample tested may be normal or abnormal as stated in claim 3. Chupp et al. also describe anemic patients with increased reticulocyte counts as indicating rapid erythroid turnover suggesting acute blood loss or hemolysis (col. 1, lines 62-65) as stated in claims 5 and 6. However, Chupp et al. do not teach the presence of an extracellular hemoglobin product or oxygen-carrying blood substitute such as recombinant human hemoglobin, isolation and purification from animal blood, subtraction of the blood substitute correction factor from the original reported chemistry result, or cell-by-cell measurements.

Chang et al. describe hemoglobin which carries oxygen to tissues (col. 2, lines 40-43) and the use of modified hemoglobin blood substitutes as alternatives to human donor blood, such as recombinant human hemoglobin (col. 3, lines 61-63) which is an extracellular hemoglobin product or oxygen-carrying blood substitute, as stated in instant claims 2, 7, 10, and 17. Chang et al. describe adding modified hemoglobin blood substitutes to a human plasma sample with a centrifugation step (abstract) which represents isolation and purification of animal blood (as stated in instant claims 8, 11, and 18), as stated in instant claims 1 and 9. Chang et al. do not

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describe the subtraction of the blood substitute correction factor from the original reported chemistry result or cell-by-cell measurements.

Samsoondar describes a method of identifying and quantifying the concentration of a blood substitute in a sample (abstract). Samsoondar describes a method of taking the measured concentration of the blood substitute and correcting for its effect on a measured analyte concentration, such as serum/plasma total protein (abstract). Samsoondar describes making the necessary adjustment or correction to the measured analyte concentration to remove the effect of the blood substitute (page 5, lines 5-9) which represents a subtraction of the blood substitute correction factor from the original reported chemistry result, as stated in instant claims 16 and 23. Figure 3 (with the linear calibration mathematical formula) provides results of a linear regression fit of data generated from true Hb calibration (fitted Hb value) in the presence of cross-linked hemoglobin (blood substitute) and other interferents (actual Hb value) (page 5, lines 20-22) which represents a correction factor multiplied by the hemoglobin value scaled to the appropriate units of dimensions of the reported analytes to correct for interference, as stated in instant claim 16 and 23. Samsoondar describes quantifying the relationship between measured amounts of each analyte with respect to the blood substitute present in the serum or plasma specimen (page 18, lines 23-26). In an example, Samsoondar describes finding the actual serum total hemoglobin concentration by subtracting the blood substitute times the slope of the regression line (correction factor) from the measured value (page 23, lines 4-15). Samsoondar describes determining the concentration of true hemoglobin in the presence of blood substitutes (abstract). Samsoondar describes using samples contained in labeled tubes in a blood analyzer (abstract). Samsoondar describes a user can specify a particular interferent to be analyzed (page

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11, lines 2-4). Samsoondar describes screening samples by taking successive sample measurements for interferences and blood substitutes (page 11, second paragraph).

Rodriguez et al. describe a blood analyzing instrument (abstract) and taking measurements on every cell where measurement data are processed to yield a report of cells and cellular hemoglobin information including mean volumes for a sample (col. 13, lines 20-33). Rodriguez et al. describe measuring cell-by-cell hemoglobin (col. 13, lines 34-42), as stated in instant claims 1, 9, and 15. Rodriguez et al. describe analyzing whole blood, analyzing subsets of red blood cells (col. 5, line 53 to col. 6, line 51) as well as analyzing only red cells and platelets (col. 6, lines 52-59).

Chupp et al. describe the presence of classes and subclasses of red blood cells (col. 3, lines 53-54) and how the two methods used can distinguish cells and subdivide the cell types into finer classifications (col. 3, lines 7-14). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Chupp et al. by use of an extracellular hemoglobin product or oxygen-carrying blood substitute, as taught by Chang et al., where the motivation would have been to screen human blood and plasma to determine the safety of modified hemoglobin blood substitutes for humans, as stated by Chang et al. (col. 4, lines 11-30). It would have been further obvious to subtract the blood substitute correction factor from the originally reported chemistry result, as taught by Samsoondar, in the methods of Chupp et al. and Chang et al. where the motivation would have been to determine the concentration of true hemoglobin in the presence of blood substitutes, as stated by Samsoondar (abstract). It would have been further obvious to measure cell-by-cell hemoglobin as taught by Rodriguez et al. in the methods of Chupp et al., Chang et al., and Samsoondar, where the motivation would

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have been to determine a thorough analysis of a blood sample regarding various blood parameters, as stated by Rodríguez et al. (col. 1, lines 39-47 and col. 13, lines 20-33) by increasing the precision and accuracy of previous manual methods of hematology analysis by using automated systems (Chupp et al., col. 7, lines 11-16), and enhancing the understanding of safety and potential problems of the various types of blood and blood substitutes in humans at the time of the invention, as stated by Chang et al. (col. 4, lines 11-30).

Thus, Chupp et al., in view of Chang et al., Samsoondar, and Rodriguez et al., motivate the limitations in claims 1-3 and 5-24 of the instant invention.

Applicant summarizes the invention.

Chupp et al.

Applicant summarizes the Chupp et al. reference and argues that hemoglobin is measured after the red blood cells are lysed. This statement is found unpersuasive as the instant claims state do not specify when hemoglobin is measured. It is noted that intracellular can be interpreted to be anything originally from the cell as opposed to a blood substitute which does not originate from the cell (extracellular). Furthermore, it is noted that the instant claims 1 and 9 state “without separation of said red blood cells from said extracellular heme-colored blood substitute *prior* to analysis” which does not exclude separation or lysing occurring *during* analysis. Applicant argues that were one to hypothetically employ a blood sample comprising both intracellular and extracellular hemoglobin in the method of Chupp et al., a correct

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intracellular hemoglobin measurement could not be obtained. While instant claims 1 and 9 indicate there is no separation of RBCs from extracellular heme-colored blood substitute “prior to analysis”, it is noted that the claims do not exclude separation of these components *during* analysis, as noted in some of the prior art references that recite red blood cell features or plasma features, suggesting that one could reasonably arrive at measurements involving intracellular hemoglobin. Applicant argues that there is simply no teaching of a method of measuring “intracellular” hemoglobin in the presence of extracellular hemoglobin or heme-colored blood substitute. This statement is found unpersuasive as Chupp et al. measure intracellular hemoglobin while other references provide limitations for the extracellular components in the instant claims. Applicant argues that the measurement of intracellular hemoglobin must be hemoglobin inside a blood cell at the time of the measurement. This statement is found unpersuasive as Applicant is adding limitations to the term “intracellular” which are narrower and not specifically recited in the claims. Applicant agrees that Chupp et al. disclose hemoglobin which is intracellular in origin. Applicant argues that Chupp et al. do not distinguish this “intracellular” hemoglobin from hemoglobin or hemoglobin substitutes that were present outside of red cells prior to their being lysed. This statement is found unpersuasive as Chupp et al. is used in a 35 USC 103(a) rejection and need not cover claim limitations that are described by the other references in this rejection.

Chang et al.

Applicant summarizes the Chang et al. reference having a blood substitute added to the plasma sample and argues that Chang et al. do not describe a sample comprising intracellular and extracellular hemoglobin. This statement is found unpersuasive as the blood substitute

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represents extracellular hemoglobin. Furthermore, Chang et al. do not need to describe every claim limitation since their reference is in a 35 USC 103 rejection as opposed to a 35 USC 102 rejection.

Rodriguez et al.

Applicant summarizes the Rodriguez et al. reference and argues that Rodriguez et al. do not disclose measuring the level of intracellular hemoglobin in the presence of extracellular hemoglobin. This statement is found unpersuasive as the Rodriguez et al. reference was not relied upon for this limitation.

Samsoondar

Applicant summarizes the Samsoondar reference and argues that Samsoondar does not disclose measuring the level of intracellular hemoglobin in the presence of extracellular hemoglobin. This statement is found unpersuasive as Chupp et al. describe measuring intracellular hemoglobin levels and Samsoondar describe determining the true hemoglobin concentration in the presence of blood substitutes (abstract). Applicant argues that Samsoondar teaches away from the present invention by requiring separation of red blood cells from serum or plasma prior to the measurement of hemoglobin. This statement is found unpersuasive as the instant claims recite “without separation of said red blood cells from said extracellular heme-colored blood substitute prior to analysis” which does not specify which “analysis” is being referred. Furthermore, the limitation “prior to analysis” is not necessarily done by the analyzer on line 9 of instant claim 1, since it is unclear to which “analysis” is being referred. It is further noted that these claims exclude separation prior to analysis, but not *during* analysis.

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Applicant argues that there is no motivation to combine the references. This statement is found unpersuasive as motivational statements are provided for combining the individual references together, as set forth in the rejection above. Applicant argues that the statement “would have expected success to combine these references, because the prior art references all deal with analyzing blood samples” is not a motivation to combine. It is noted that this statement is an expectation of success statement that differs from a motivation statement. Applicant’s arguments are deemed unpersuasive for the reasons given above.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Ardin Marschel, can be reached on (571) 272-0718.

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Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

April 12, 2006

A handwritten signature in cursive script, appearing to read 'Carolyn Smith', written in black ink.

Carolyn Smith
Examiner
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